Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1644pnh

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 4	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS 5	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 6	MAY 11	KOREAPAT updates resume
NEWS 7	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS 8	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 9	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS 10	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS 11	JUN 26	TULSA/TULSA2 reloaded and enhanced with new search and and display fields
NEWS 12	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 13	JUl 07	Coverage of Research Disclosure reinstated in DWPI
NEWS 14	JUl 11	CHEMSAFE reloaded and enhanced

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 18:32:59 ON 12 JUL 2006

=> file medline embase biosis scisearch caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 18:33:17 ON 12 JUL 2006

FILE 'EMBASE' ENTERED AT 18:33:17 ON 12 JUL 2006

FILE 'BIOSIS' ENTERED AT 18:33:17 ON 12 JUL 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'SCISEARCH' ENTERED AT 18:33:17 ON 12 JUL 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 18:33:17 ON 12 JUL 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> s conjugate
L1 264529 CONJUGATE

=> s l1 and superantigen
L2 185 L1 AND SUPERANTIGEN

=> s l2 and binds class II
L3 0 L2 AND BINDS CLASS II

=> s l2 and notch ligand
L4 1 L2 AND NOTCH LIGAND

=> d l4 cbib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
2003:118018 Document No. 138:168835 Targeting of an antigen presenting cell (APC) with a modulator of T cell signalling, such as a Notch ligand, coupled to the MHC class II-binding motif from a superantigen. Bodmer, Mark William; Champion, Brian Robert; McKenzie, Grahame James; Nye, Lucy Emma (Lorantis Limited, UK). PCT Int. Appl. WO 2003012111 A2 20030213, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3381 20020725. PRIORITY: GB 2001-18155 20010725.

AB The present invention relates to the concept of delivering a modulator of T cell signaling, such as a Notch ligand, to an antigen presenting cell (APC). The targeting approach disclosed uses, for example, the major histocompatibility complex (MHC) class II binding motif from a superantigen coupled to a modulator of the Notch signaling pathway. Superantigens bind both MHC class II mols. and subsets of T cell receptors and thus effectively cross-link APCs to T cells and activate cells polyclonally. The mol. regions of these mols. that impart T cell receptor (TCR) and MHC class II binding have been defined structurally and have been shown to be distinct regions of the mol. By using the MHC class II binding domain with a modulator of the Notch signaling pathway we can focus the activity of the Notch signaling pathway modulator to the APCs at the site of delivery. Further, the domain lacks toxin activity because it cannot find the T cell receptor to activate T cells. According to one aspect of the present invention there is provided a conjugate comprising a first and a second sequence wherein the first sequence comprises a polypeptide which is capable of binding to an APC, or a polynucleotide encoding therefor, and the second sequence comprises a polypeptide comprising a modulator of a signaling pathway in a T cell or a polynucleotide encoding therefor.

=> s l1 and superantigen

L5 185 L1 AND SUPERANTIGEN

=> s l5 and class II binding motif
L6 1 L5 AND CLASS II BINDING MOTIF

=> d l6 cbib abs

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
2003:118018 Document No. 138:168835 Targeting of an antigen presenting cell (APC) with a modulator of T cell signalling, such as a Notch ligand, coupled to the MHC class II-binding motif from a superantigen. Bodmer, Mark William; Champion, Brian Robert; McKenzie, Grahame James; Nye, Lucy Emma (Lorantis Limited, UK). PCT Int. Appl. WO 2003012111 A2 20030213, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3381 20020725. PRIORITY: GB 2001-18155 20010725.

AB The present invention relates to the concept of delivering a modulator of T cell signaling, such as a Notch ligand, to an antigen presenting cell (APC). The targeting approach disclosed uses, for example, the major histocompatibility complex (MHC) class II binding motif from a superantigen coupled to a modulator of the Notch signaling pathway. Superantigens bind both MHC class II mols. and subsets of T cell receptors and thus effectively cross-link APCs to T cells and activate cells polyclonally. The mol. regions of these mols. that impart T cell receptor (TCR) and MHC class II binding have been defined structurally and have been shown to be distinct regions of the mol. By using the MHC class II binding domain with a modulator of the Notch signaling pathway we can focus the activity of the Notch signaling pathway modulator to the APCs at the site of delivery. Further, the domain lacks toxin activity because it cannot find the T cell receptor to activate T cells. According to one aspect of the present invention there is provided a conjugate comprising a first and a second sequence wherein the first sequence comprises a polypeptide which is capable of binding to an APC, or a polynucleotide encoding therefor, and the second sequence comprises a polypeptide comprising a modulator of a signaling pathway in a T cell or a polynucleotide encoding therefor.

=> s l1 and MHC class II binding peptide
L7 3 L1 AND MHC CLASS II BINDING PEPTIDE

=> dup remove l7
PROCESSING COMPLETED FOR L7
L8 3 DUP REMOVE L7 (0 DUPLICATES REMOVED)

=> d l8 1-3 cbib abs

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
2002:369020 Document No. 136:380098 MHC binding peptide oligomers, production, and therapeutic use. Strominger, Jack L.; Falk, Kirsten; Rotzschke, Olaf (USA). U.S. Pat. Appl. Publ. US 2002058787 A1 20020516, 29 pp., Cont.-in-part of U.S. Ser. No. 692,167, abandoned. (English). CODEN: USXXCO. APPLICATION: US 1999-245487 19990205. PRIORITY: US 1996-692167 19960805; WO 1997-US13885 19970805.

AB Oligomers are disclosed which comprise at least two MHC binding peptides joined by a flexible mol. linker. The MHC binding peptides can be MHC class I binding peptides or MHC class II

binding peptides. Also disclosed is an oriented cloning method for producing such oligomers. The disclosed oligomers can be used e.g. in connection with methods for specifically activating or inhibiting the activation of CD4+ or CD8+ T cells. Such methods provide therapeutic approaches for the treatment of tumors, autoimmune disorders, allograft rejection and allergic reactions.

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

2002:947513 Document No. 138:217156 Lipoconjugates for the noncovalent generation of microarrays in biochemical and cellular assays. Hoff, Antje; Andre, Thomas; Schaffer, Tilman E.; Jung, Gunther; Wiesmuller, Karl-Heinz; Brock, Roland (Group of Genomics and Proteomics, Center for Bioinformatics Tubingen, Institute for Cell Biology, University of Tubingen, Tubingen, 72076, Germany). ChemBioChem, 3(12), 1183-1191 (English) 2002. CODEN: CBCHFX. ISSN: 1439-4227. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA.

AB The generation of microarrays by functionalization of hydrophobic glass surfaces with conjugates of triacylated lipophilic end-groups and with a peptide or hapten as a test substance is presented. Immobilization on the hydrophobic surfaces through the triacylated anchor group is fully orthogonal to the reactivity of functional groups within the test substances. The technique is therefore free of risk that reactions of these functional groups may influence the biol. activity of the test compds. in screening applications. In addition, no preactivation of either the surface or the compds. is required. Reagents and substrates may be stored at ambient conditions for long periods of time. The lipoconjugates are administered from aqueous solution enabling automated nanopipetting down to spot dimensions of 100 μm across. The microstructures are stable with respect to the conditions of biochem. assays and applications in cell biol. Due to the hydrophobicity of the nonfunctionalized surfaces, standard blocking protocols used in microtiter-plate testing can be employed, thereby inhibiting nonspecific binding of assay reagents. Generation of these microstructures on hydrophobic glass slides or coverslips enables highly sensitive multichannel read-outs with high-resolution fluorescence microscopy.

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

2002:11785 Document No. 136:193745 Quinolone-photoconjugated major histocompatibility complex class II-binding peptides with lysine are antigenic for T cells mediating murine quinolone photoallergy. Tokura, Yoshiki; Seo, Naohiro; Fujie, Michio; Takigawa, Masahiro (Department of Dermatology, Hamamatsu University School of Medicine, Hamamatsu, 431-3192, Japan). Journal of Investigative Dermatology, 117(5), 1206-1211 (English) 2001. CODEN: JIDEAE. ISSN: 0022-202X. Publisher: Blackwell Science, Inc..

AB Fluoroquinolone antibacterial agents cause photosensitivity dermatitis as an adverse effect and can function immunol. as photohapten. In a murine model of quinolone photoallergy, Langerhans cells are photomodified with a systemically given quinolone upon UV A irradiation of skin and thus present photohaptenic moieties to sensitize and restimulate T cells. The aim of this study is to determine the site of peptides/proteins photobound to quinolones and to assess the T cell antigenicity of quinolone-photocoupled peptides using Langerhans cells as photoadduct-presenting cells. On an amino acid composition anal., lysine was preferentially degraded in bovine serum albumin that was UV A-conjugated with a representative quinolone ofloxacin. An affinity chromatog. study using a quinolone photoadduct-specific monoclonal antibody as ligand demonstrated preferential photocoupling of ofloxacin with a lysine-containing peptide. CD4+ T cells were purified from lymph nodes of BALB/c mice sensitized s.c. with ofloxacin-photomodified epidermal cells and from those sensitized epicutaneously via barrier-disrupted skin with a major histocompatibility complex class II (I-Ad)-binding, ofloxacin-photoconjugated peptide. These immune T cells proliferated in vitro in response to Langerhans cells loaded with class II-binding, lysine-containing peptides when photomodified with ofloxacin. Furthermore, epicutaneous application of the

ofloxacin-photoconjugated peptide was able to prime mice for subsequent elicitation of photoallergy evoked with systemic ofloxacin and UV A light. This study suggests that lysine affords quinolone photocoupling of peptides and quinolone-photomodified peptides on class II mols. stimulate pathogenetic T cells in quinolone photoallergy.

=> s l1 and notch ligand
L9 8 L1 AND NOTCH LIGAND

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 8 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> d l10 1-8 cbib abs

L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2005:120966 Document No. 142:213330 Purification of Notch receptor ligand proteins by hydrophobic interaction chromatography. Dosanjh, Bhupinder (Lorantis Limited, UK). PCT Int. Appl. WO 2005012349 A2 20050210, 66 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB3327 20040730. PRIORITY: WO 2003-GB3285 20030801; GB 2004-2208 20040131; GB 2004-2562 20040205.
AB Methods for purifying Notch ligand proteins and fragments, variants or derivs. without the use of affinity ligand peptides is described. Specifically, methods of hydrophobic interaction chromatog. (HIC) using hydrophobic derivs. of agarose and silica are used in combination with other chromatog. methods. The purified proteins are free of endotoxins and DNA and may be suitable for therapeutic use (no data.). An N-terminal 332-amino acid fragment of human Delta-1 protein was synthesized in CHO-K1 cells. Purification of the protein by HIC on Bu Sepharose 4FF resulted in a rapid purification of the protein.

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1171811 Document No. 144:365540 Preparation of polymer matrix bioconjugated with Notch ligand. Konno, Tomohiro; Sakano, Seiji; Tohda, Shuji; Ito, Yoshihiro (Regenerative Med. Bioreactor Project, Kanagawa Acad. Sci. Technology, Japan). Ensho, Saisei, 25(5), 426-430 (Japanese) 2005. CODEN: ENSHCC. ISSN: 1346-8022. Publisher: Nippon Ensho-Saisei Igakkai.
AB A review. It is important to prepare the cell culture devices with functional polymer surfaces. Notch ligand delta-1 is considered as one of the important membrane proteins for self-renewal of hematopoietic stem cells. In this study, a polymer matrix immobilized with Notch ligand delta-1 was prepared by photo-immobilization technique for culture the stem cells. It has been reported that photo-reactive polymers bearing azidophenyl groups could immobilize functional proteins without losing their biol. activity. Therefore, a novel photo-reactive phospholipid polymer, 2-methacryloyloxyethyl phosphorylcholine polymer bearing azidophenyl groups, was applied as the matrix to conjugate with Notch ligand delta-1. A leukemia cell line, TMD7, was cultured on the bioconjugated polymer surface. The polymer surface immobilized with Notch ligand delta-1 was recognized by TMD7, and the cells efficiently grow on the phospholipid polar group concentrated surface (PC surface) with protein. It was considered that the PC surface provided a suitable environment around the membrane proteins without denaturation. The photo-reactive phospholipid polymer was

expected to constitute on in vitro niche to culture hematopoietic stem cells.

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2004:718374 Document No. 141:242022 Modulators of Notch signalling and of immune cell costimulatory activity for immunotherapy of inflammation, asthma, allergy, transplant rejection, graft versus host disease or autoimmune disease. Champion, Brian Robert; Lioumi, Maria; McKenzie, Grahame James (Lorantis Limited, UK). PCT Int. Appl. WO 2004073732 A1 20040902, 157 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB668 20040218. PRIORITY: GB 2003-3663 20030218.
AB A method is described for detecting, measuring or monitoring Notch signaling by determining the amount of an immune cell costimulatory protein, polypeptide or polynucleotide or determining the amount of a polynucleotide coding for such a protein or polypeptide. The Notch signaling modulators of the invention comprise Notch ligand DSL domain or intracellular domain. The immune cell costimulatory proteins are CD28, CD80, CD86, CTLA-4, ICOS, ICOS ligand, CD40, CD40L, PD-1, PD-L1, PD-L2, OX40 or OX40L. Methods of modulating the immune system are also described. The Notch signaling modulators and the immune cell costimulatory activity modulators are useful for increasing or reducing immune response against cancer or inflammation, allergy, asthma, graft vs. host disease, autoimmune disease and transplant rejection.

L10 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2004:633546 Document No. 141:179617 Treatment of autoimmune diseases using an activator for the notch signaling pathway. Champion, Brian Robert; Ragno, Silvia; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004064863 A1 20040805, 244 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB263 20040123. PRIORITY: GB 2003-1519 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1512 20030123; GB 2003-1510 20030123; GB 2003-1521 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-1529 20030123; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003; WO 2004-GB46 20040107.
AB A product is disclosed comprising a modulator of the Notch signaling pathway; and an autoantigen or bystander antigen, or a polynucleotide coding for an autoantigen or bystander antigen; as a combined preparation for simultaneous, contemporaneous, sep. or sequential use for modulation of immune response. The invention relates to modulators of notch signalling pathway for T cell activation, and therapeutic use in immunosuppression. In the examples of the invention, a fusion protein comprising the extracellular domain of human Delta1 ligand fused to the Fc domain of human IgG4.

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2004:589350 Document No. 141:145678 Particle-bound modulators of the Notch signaling pathway for use in the treatment of disorders of the immune

system. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; McKenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004060262 A2 20040722, 294 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB46 20040107. PRIORITY: GB 2003-234 20030107; GB 2003-1519 20030123; GB 2003-1510 20030123; GB 2003-1512 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1521 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1529 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-6621 20030322; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003.

AB Modulators of Notch signaling are immobilized on pharmaceutically acceptable carriers for therapeutic use in the treatment of immune disorders. Two derivs. of the Notch ligand Delta were prepared: a fusion protein with IgG4 and a cysteine-rich derivative These were immobilized on Dynabeads or polystyrene latex either by chemical crosslinking or by binding to an antibody to the IgG4 domain. The particle-bound ligands stimulated interleukin 10 secretion and inhibited interleukin 5 secretion in a mixed lymphocyte reaction using PBMCs from healthy donors.

L10 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2004:252539 Document No. 140:286167 Derivatives of Notch receptors ligand proteins for use as immunomodulators acting on T cells. Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara (Lorantis Limited, UK). PCT Int. Appl. WO 2004024764 A1 20040325, 145 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB3908 20030909. PRIORITY: GB 2002-20912 20020910; GB 2002-20913 20020910; WO 2002-GB5133 20021113; WO 2002-GB5137 20021113; GB 2003-234 20030107; WO 2003-GB1525 20030404; WO 2003-GB3285 20030801.

AB Derivs. of Notch receptors ligands, such as Delta-like 1, that include the DSL domain, 1-5 EGF repeat domains, and the N-terminal ligand domain fused to a second peptide are described for use in modifying an immune response. A series of derivs. of the Delta-like 1 Notch ligand containing 2-7 EGF repeats fused a human IgG Fc domain were constructed by standard methods. The shorter deletion derivs. were able to strongly induce a Notch signaling. Jagged-1 deletion derivs. antagonizing Notch signaling are also demonstrated.

L10 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2003:837139 Document No. 139:336935 Particle-bound Notch pathway-modifying immunomodulators for immunotherapy of cancer, allergy, infection, inflammation, and autoimmune disease and for modulator screening. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003087159 A2 20031023, 177 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU,

MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB1525 20030404. PRIORITY: GB 2002-7930 20020405; GB 2002-7929 20020405; GB 2002-12282 20020528; GB 2002-12283 20020528; WO 2002-GB3397 20020725; WO 2002-GB3426 20020725; GB 2002-20913 20020910; GB 2002-20912 20020910; GB 2003-234 20030107.

AB A method is disclosed for therapeutic modulation of Notch signalling by administering modulators of the Notch signal transduction pathway bound to a pharmaceutically acceptable carrier. The modulators may be in mixts. of up to 100 different entities. The modulators may also be conjugated with one another, e.g. in fusion proteins. The construction of a CHO-derived cell line carrying a Notch pathway-dependent luciferase reporter gene to screen for Notch ligands is described.

L10 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2003:118018 Document No. 138:168835 Targeting of an antigen presenting cell (APC) with a modulator of T cell signalling, such as a Notch ligand, coupled to the MHC class II-binding motif from a superantigen. Bodmer, Mark William; Champion, Brian Robert; McKenzie, Grahame James; Nye, Lucy Emma (Lorantis Limited, UK). PCT Int. Appl. WO 2003012111 A2 20030213, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3381 20020725. PRIORITY: GB 2001-18155 20010725.

AB The present invention relates to the concept of delivering a modulator of T cell signaling, such as a Notch ligand, to an antigen presenting cell (APC). The targeting approach disclosed uses, for example, the major histocompatibility complex (MHC) class II binding motif from a superantigen coupled to a modulator of the Notch signaling pathway. Superantigens bind both MHC class II mols. and subsets of T cell receptors and thus effectively cross-link APCs to T cells and activate cells polyclonally. The mol. regions of these mols. that impart T cell receptor (TCR) and MHC class II binding have been defined structurally and have been shown to be distinct regions of the mol. By using the MHC class II binding domain with a modulator of the Notch signaling pathway we can focus the activity of the Notch signaling pathway modulator to the APCs at the site of delivery. Further, the domain lacks toxin activity because it cannot find the T cell receptor to activate T cells. According to one aspect of the present invention there is provided a conjugate comprising a first and a second sequence wherein the first sequence comprises a polypeptide which is capable of binding to an APC, or a polynucleotide encoding therefor, and the second sequence comprises a polypeptide comprising a modulator of a signaling pathway in a T cell or a polynucleotide encoding therefor.

```
=> s notch ligand conjugate
L11          0 NOTCH LIGAND CONJUGATE

=> s notch ligand
L12       1900 NOTCH LIGAND

=> s l12 and conjugate
L13          8 L12 AND CONJUGATE

=> dup remove l13
PROCESSING COMPLETED FOR L13
L14          8 DUP REMOVE L13 (0 DUPLICATES REMOVED)

=> d l14 1-8 cbib abs
```

L14 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2005:120966 Document No. 142:213330 Purification of Notch receptor ligand proteins by hydrophobic interaction chromatography. Dosanjh, Bhupinder (Lorantis Limited, UK). PCT Int. Appl. WO 2005012349 A2 20050210, 66 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB3327 20040730. PRIORITY: WO 2003-GB3285 20030801; GB 2004-2208 20040131; GB 2004-2562 20040205.

AB Methods for purifying Notch ligand proteins and fragments, variants or derivs. without the use of affinity ligand peptides is described. Specifically, methods of hydrophobic interaction chromatog. (HIC) using hydrophobic derivs. of agarose and silica are used in combination with other chromatog. methods. The purified proteins are free of endotoxins and DNA and may be suitable for therapeutic use (no data.). An N-terminal 332-amino acid fragment of human Delta-1 protein was synthesized in CHO-K1 cells. Purification of the protein by HIC on Bu Sepharose 4FF resulted in a rapid purification of the protein.

L14 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1171811 Document No. 144:365540 Preparation of polymer matrix bioconjugated with Notch ligand. Konno, Tomohiro; Sakano, Seiji; Tohda, Shuji; Ito, Yoshihiro (Regenerative Med. Bioreactor Project, Kanagawa Acad. Sci. Technology, Japan). Ensho, Saisei, 25(5), 426-430 (Japanese) 2005. CODEN: ENSHCC. ISSN: 1346-8022. Publisher: Nippon Ensho-Saisei Igakkai.

AB A review. It is important to prepare the cell culture devices with functional polymer surfaces. Notch ligand delta-1 is considered as one of the important membrane proteins for self-renewal of hematopoietic stem cells. In this study, a polymer matrix immobilized with Notch ligand delta-1 was prepared by photo-immobilization technique for culture the stem cells. It has been reported that photo-reactive polymers bearing azidophenyl groups could immobilize functional proteins without losing their biol. activity. Therefore, a novel photo-reactive phospholipid polymer, 2-methacryloyloxyethyl phosphorylcholine polymer bearing azidophenyl groups, was applied as the matrix to conjugate with Notch ligand delta-1. A leukemia cell line, TMD7, was cultured on the bioconjugated polymer surface. The polymer surface immobilized with Notch ligand delta-1 was recognized by TMD7, and the cells efficiently grow on the phospholipid polar group concentrated surface (PC surface) with protein. It was considered that the PC surface provided a suitable environment around the membrane proteins without denaturation. The photo-reactive phospholipid polymer was expected to constitute on in vitro niche to culture hematopoietic stem cells.

L14 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
2004:718374 Document No. 141:242022 Modulators of Notch signalling and of immune cell costimulatory activity for immunotherapy of inflammation, asthma, allergy, transplant rejection, graft versus host disease or autoimmune disease. Champion, Brian Robert; Lioumi, Maria; McKenzie, Grahame James (Lorantis Limited, UK). PCT Int. Appl. WO 2004073732 A1 20040902, 157 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR,

GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB668 20040218. PRIORITY: GB 2003-3663 20030218.

AB A method is described for detecting, measuring or monitoring Notch signaling by determining the amount of an immune cell costimulatory protein, polypeptide or polynucleotide or determining the amount of a polynucleotide coding for such a protein or polypeptide. The Notch signaling modulators of the invention comprise Notch ligand DSL domain or intracellular domain. The immune cell costimulatory proteins are CD28, CD80, CD86, CTLA-4, ICOS, ICOS ligand, CD40, CD40L, PD-1, PD-L1, PD-L2, OX40 or OX40L. Methods of modulating the immune system are also described. The Notch signaling modulators and the immune cell costimulatory activity modulators are useful for increasing or reducing immune response against cancer or inflammation, allergy, asthma, graft vs. host disease, autoimmune disease and transplant rejection.

L14 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2004:633546 Document No. 141:179617 Treatment of autoimmune diseases using an activator for the notch signaling pathway. Champion, Brian Robert; Ragno, Silvia; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004064863 A1 20040805, 244 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB263 20040123. PRIORITY: GB 2003-1519 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1512 20030123; GB 2003-1510 20030123; GB 2003-1521 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-1529 20030123; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003; WO 2004-GB46 20040107.

AB A product is disclosed comprising a modulator of the Notch signaling pathway; and an autoantigen or bystander antigen, or a polynucleotide coding for an autoantigen or bystander antigen; as a combined preparation for simultaneous, contemporaneous, sep. or sequential use for modulation of immune response. The invention relates to modulators of notch signalling pathway for T cell activation, and therapeutic use in immunosuppression. In the examples of the invention, a fusion protein comprising the extracellular domain of human Delta1 ligand fused to the Fc domain of human IgG4.

L14 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2004:589350 Document No. 141:145678 Particle-bound modulators of the Notch signaling pathway for use in the treatment of disorders of the immune system. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; McKenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004060262 A2 20040722, 294 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB46 20040107. PRIORITY: GB 2003-234 20030107; GB 2003-1519 20030123; GB 2003-1510 20030123; GB 2003-1512 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1521 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1529 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-6621 20030322; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO

2003-GB3285 20030801; GB 2003-23130 20031003.

AB Modulators of Notch signaling are immobilized on pharmaceutically acceptable carriers for therapeutic use in the treatment of immune disorders. Two derivs. of the Notch ligand Delta were prepared: a fusion protein with IgG4 and a cysteine-rich derivative These were immobilized on Dynabeads or polystyrene latex either by chemical crosslinking or by binding to an antibody to the IgG4 domain. The particle-bound ligands stimulated interleukin 10 secretion and inhibited interleukin 5 secretion in a mixed lymphocyte reaction using PBMCs from healthy donors.

L14 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2004:252539 Document No. 140:286167 Derivatives of Notch receptors ligand proteins for use as immunomodulators acting on T cells. Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara (Lorantis Limited, UK). PCT Int. Appl. WO 2004024764 A1 20040325, 145 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB3908 20030909. PRIORITY: GB 2002-20912 20020910; GB 2002-20913 20020910; WO 2002-GB5133 20021113; WO 2002-GB5137 20021113; GB 2003-234 20030107; WO 2003-GB1525 20030404; WO 2003-GB3285 20030801.

AB Derivs. of Notch receptors ligands, such as Delta-like 1, that include the DSL domain, 1-5 EGF repeat domains, and the N-terminal ligand domain fused to a second peptide are described for use in modifying an immune response. A series of derivs. of the Delta-like 1 Notch ligand containing 2-7 EGF repeats fused a human IgG Fc domain were constructed by standard methods. The shorter deletion derivs. were able to strongly induce a Notch signaling. Jagged-1 deletion derivs. antagonizing Notch signaling are also demonstrated.

L14 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2003:837139 Document No. 139:336935 Particle-bound Notch pathway-modifying immunomodulators for immunotherapy of cancer, allergy, infection, inflammation, and autoimmune disease and for modulator screening. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003087159 A2 20031023, 177 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB1525 20030404. PRIORITY: GB 2002-7930 20020405; GB 2002-7929 20020405; GB 2002-12282 20020528; GB 2002-12283 20020528; WO 2002-GB3397 20020725; WO 2002-GB3426 20020725; GB 2002-20913 20020910; GB 2002-20912 20020910; GB 2003-234 20030107.

AB A method is disclosed for therapeutic modulation of Notch signalling by administering modulators of the Notch signal transduction pathway bound to a pharmaceutically acceptable carrier. The modulators may be in mixts. of up to 100 different entities. The modulators may also be conjugated with one another, e.g. in fusion proteins. The construction of a CHO-derived cell line carrying a Notch pathway-dependent luciferase reporter gene to screen for Notch ligands is described.

L14 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

2003:118018 Document No. 138:168835 Targeting of an antigen presenting cell (APC) with a modulator of T cell signalling, such as a Notch

ligand, coupled to the MHC class II-binding motif from a superantigen. Bodmer, Mark William; Champion, Brian Robert; McKenzie, Grahame James; Nye, Lucy Emma (Lorantis Limited, UK). PCT Int. Appl. WO 2003012111 A2 20030213, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3381 20020725. PRIORITY: GB 2001-18155 20010725.

AB The present invention relates to the concept of delivering a modulator of T cell signaling, such as a Notch ligand, to an antigen presenting cell (APC). The targeting approach disclosed uses, for example, the major histocompatibility complex (MHC) class II binding motif from a superantigen coupled to a modulator of the Notch signaling pathway. Superantigens bind both MHC class II mols. and subsets of T cell receptors and thus effectively cross-link APCs to T cells and activate cells polyclonally. The mol. regions of these mols. that impart T cell receptor (TCR) and MHC class II binding have been defined structurally and have been shown to be distinct regions of the mol. By using the MHC class II binding domain with a modulator of the Notch signaling pathway we can focus the activity of the Notch signaling pathway modulator to the APCs at the site of delivery. Further, the domain lacks toxin activity because it cannot find the T cell receptor to activate T cells. According to one aspect of the present invention there is provided a conjugate comprising a first and a second sequence wherein the first sequence comprises a polypeptide which is capable of binding to an APC, or a polynucleotide encoding therefor, and the second sequence comprises a polypeptide comprising a modulator of a signaling pathway in a T cell or a polynucleotide encoding therefor.

=> s (bodmer m?/au or champion b?/au or mckenzie g?/au or nye l?/au)
L15 1323 (BODMER M?/AU OR CHAMPION B?/AU OR MCKENZIE G?/AU OR NYE L?/AU)

=> s l15 and notch ligand
L16 21 L15 AND NOTCH LIGAND

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17 20 DUP REMOVE L16 (1 DUPLICATE REMOVED)

=> d l17 1-20 cbib abs

L17 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
2006:559208 Modulators of Notch signaling and cytokine expression for immunotherapy of inflammation and autoimmune disease. Champion, Brian Robert; Young, Lesley Lynn; Mckenzie, Grahame James (UK). U.S. Pat. Appl. Publ. US 20060128619 A1 20060615, 92 pp. (English). CODEN: USXXCO. APPLICATION: US 2005-178724 20050711. PRIORITY: GB 2003-428 20030109; WO 2004-GB21 20040109.

AB The invention provides a method for modifying IL-4 expression in a cell using a modulator of Notch signaling. It also provides methods for generating immune modulatory cytokine profiles with increased IL-4 expression and/or increased IL-10 expression and/or reduced IL-5, IL-13 and TNFα expression. In addition, the invention provides a method for increasing a TH2 immune response and/or decreasing a TH1 immune response in a cell, using a modulator of Notch signaling. The modulators of Notch signaling comprise Notch receptor agonists or antagonists, particularly fusion proteins comprising DSL or EGF domains from Delta or Jagged proteins and an Ig Fc segment. Alternatively, the modulator of Notch signaling comprises a Notch intracellular domain. The invention also claims polynucleotides encoding modulators of Notch signaling. Methods of

the invention are claimed for use in treating inflammation or an autoimmune condition. In the examples, modulation of cytokine production in mouse and human CD4+ cells by soluble or immobilized human Delta 1 extracellular domain-IgG4Fc fusion protein was measured. Expression of IL-10, IFN-γ, and transcription factors Tbet, c-Maf, and GATA-3 was measured in anti-CD3/28 activated mouse T cells under neutral, TH1, or TH2 culture conditions after treatment with the Delta1-Fc protein.

L17 ANSWER 2 OF 20 MEDLINE on STN DUPLICATE 1
2006399807. PubMed ID: 16818743. Small Interfering RNA-Mediated Knockdown of Notch Ligands in Primary CD4+ T Cells and Dendritic Cells Enhances Cytokine Production. Stallwood Yvette; Briend Emmanuel; Ray Katrina M; Ward George A; Smith Beverley J; Nye Emma; Champion Brian R; McKenzie Grahame J. (Lorantis Ltd., Cambridge, United Kingdom.) Journal of immunology (Baltimore, Md. : 1950), (2006 Jul 15) Vol. 177, No. 2, pp. 885-95. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The key interaction in the adaptive immune system's response to pathogenic challenge occurs at the interface between APCs and T cells. Families of costimulatory and coinhibitory molecules function in association with the cytokine microenvironment to orchestrate appropriate T cell activation programs. Recent data have demonstrated that the Notch receptor and its ligands also function at the APC:T interface. In this study, we describe synthetic small interfering RNA (siRNA) sequences targeting the human Notch ligands Delta1, Jagged1 and Jagged2. Transfection of these siRNAs into human primary CD4(+) T cells and monocyte-derived dendritic cells leads to knockdown of endogenous Notch ligand message. Knockdown of any one of these three Notch ligands in dendritic cells enhanced IFN-gamma production from allogeneic CD4(+) T cells in MLR. In contrast, Delta1 knockdown in CD4(+) T cells selectively enhanced production of IFN-gamma, IL-2, and IL-5 in response to polyclonal stimulation, while Jagged1 or Jagged2 knockdown had no effect. Strikingly, blockade of Notch cleavage with a gamma secretase inhibitor failed to affect cytokine production in this system, implying that Delta1 can influence cytokine production via a Notch cleavage-independent mechanism. These data show for the first time that the Notch pathway can be targeted by siRNA, and that its antagonism may be a unique therapeutic opportunity for immune enhancement.

L17 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1242709 Document No. 143:466059 Pharmaceutical compositions and medical treatments comprising notch ligand proteins. Champion, Brian Robert; Lennard, Andrew Christopher; McKenzie, Grahame James; Tugal, Tamara (UK). U.S. Pat. Appl. Publ. US 2005261477 A1 20051124, 86 pp., Cont.-in-part of Appl. No. PCT/GB03/03908. (English). CODEN: USXXCO. APPLICATION: US 2005-78735 20050310. PRIORITY: GB 2002-20912 20020910; GB 2002-20913 20020910; WO 2002-GB5137 20021113; WO 2002-GB5133 20021113; GB 2003-234 20030107; WO 2003-GB1525 20030404; WO 2003-GB3285 20030801; WO 2003-GB3908 20030909.

AB Provided is a Notch ligand protein or polypeptide comprising a Notch ligand DSL domain; 1 to 5 (but no more than 5) Notch ligand EGF repeat domains; optionally, all or part of a Notch ligand N-terminal domain; and optionally, one or more heterologous amino acid sequences. Also provided is a homogeneous or heterogeneous multimer of the protein or polypeptide and a polynucleotide encoding the Notch ligand protein or polypeptide. An immune response can be modified in a subject by administering the Notch ligand protein or polypeptide to the subject.

L17 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
2004:857429 Document No. 141:325713 Notch signalling modulation using a KLF and its effectors, diagnostic assays and therapeutics for autoimmune and inflammatory disorders. Champion, Brian Robert; Lioumi, Maria; McKenzie, Grahame James; Young, Lesley Lynn (Lorantis Limited,

UK). PCT Int. Appl. WO 2004087195 A2 20041014, 150 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB1379 20040329. PRIORITY: GB 2003-7472 20030401.

AB A method is described for detecting, measuring or monitoring Notch signalling by determining the amount of a KLF (Kruppel-like factor) protein, or determining the amount of a polynucleotide coding for KLF. Methods of modulating the immune system by modulation of KLF activity and methods of modulating immune cell quiescence and proliferation are also described. A preferred KLF is human KLF-2, also known as LKLF (Q9Y5W3, NM_016270). Modulators of the Notch signalling pathway also comprise Notch ligands , such as Delta or Jagged, and DSL, EGF-like or extracellular domains thereof and polynucleotides coding for such proteins. Sequences of Delta-1/Ig-Fc fusion proteins are provided. Notch signaling pathway modulation was demonstrated in mouse model.

L17 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2004:799474 Document No. 141:289039 Treatment of allergy using a modulator of the Notch signaling pathway along with an allergen. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James ; Ragno, Silvia; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004082710 A1 20040930, 176 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB1252 20040322. PRIORITY: GB 2003-6583 20030321; GB 2003-6582 20030321; GB 2003-6621 20030322; GB 2003-6622 20030322; GB 2003-6626 20030322; GB 2003-6624 20030322; GB 2003-6640 20030322; GB 2003-6644 20030322; GB 2003-6650 20030322; GB 2003-6651 20030322; GB 2003-6654 20030322; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003; WO 2004-GB46 20040107; WO 2004-GB263 20040123.

AB The invention provides a method for reducing an immune response to an allergen or antigenic determinant thereof in a mammal by administering a modulator of the Notch signalling pathway. The invention provides a product comprising a modulator of the Notch signalling pathway and an allergen or a polynucleotide coding for an allergen, as a combined preparation for simultaneous, contemporaneous, sep. or sequential use for promoting immune tolerance. The modulators of the Notch signalling pathway comprises Notch ligands, such as Delta or Jagged, and DSL, EGF-like or extracellular domains thereof. Sequences of Delta-1/Ig-Fc fusion proteins are provided. Notch signaling pathway modulation was demonstrated on mouse model.

L17 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2004:718374 Document No. 141:242022 Modulators of Notch signalling and of immune cell costimulatory activity for immunotherapy of inflammation, asthma, allergy, transplant rejection, graft versus host disease or autoimmune disease. Champion, Brian Robert; Lioumi, Maria; McKenzie, Grahame James (Lorantis Limited, UK). PCT Int. Appl. WO 2004073732 A1 20040902, 157 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY,

BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB668 20040218. PRIORITY: GB 2003-3663 20030218.

AB A method is described for detecting, measuring or monitoring Notch signaling by determining the amount of an immune cell costimulatory protein, polypeptide or polynucleotide or determining the amount of a polynucleotide coding for such a protein or polypeptide. The Notch signaling modulators of the invention comprise Notch ligand DSL domain or intracellular domain. The immune cell costimulatory proteins are CD28, CD80, CD86, CTLA-4, ICOS, ICOS ligand, CD40, CD40L, PD-1, PD-L1, PD-L2, OX40 or OX40L. Methods of modulating the immune system are also described. The Notch signaling modulators and the immune cell costimulatory activity modulators are useful for increasing or reducing immune response against cancer or inflammation, allergy, asthma, graft vs. host disease, autoimmune disease and transplant rejection.

L17 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2004:633546 Document No. 141:179617 Treatment of autoimmune diseases using an activator for the notch signaling pathway. Champion, Brian Robert; Ragno, Silvia; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004064863 A1 20040805, 244 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB263 20040123. PRIORITY: GB 2003-1519 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1512 20030123; GB 2003-1510 20030123; GB 2003-1521 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-1529 20030123; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003; WO 2004-GB46 20040107.

AB A product is disclosed comprising a modulator of the Notch signaling pathway; and an autoantigen or bystander antigen, or a polynucleotide coding for an autoantigen or bystander antigen; as a combined preparation for simultaneous, contemporaneous, sep. or sequential use for modulation of immune response. The invention relates to modulators of notch signalling pathway for T cell activation, and therapeutic use in immunosuppression. In the examples of the invention, a fusion protein comprising the extracellular domain of human Delta1 ligand fused to the Fc domain of human IgG4.

L17 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2004:610096 Document No. 141:156082 Methods for use of Notch signaling for modulation of cytokine production in T cells and therapeutic uses thereof. Champion, Brian Robert; Young, Lesley Lynn; McKenzie, Grahame James (Lorantis Limited, UK). PCT Int. Appl. WO 2004062686 A2 20040729, 149 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB21 20040109. PRIORITY: GB 2003-428 20030109.

AB The invention provides methods for use of modulators of Notch signaling to

regulate interleukin 4 expression and T cell immune responses. The invention further claims use of the methods for immunotherapy, to modify the TH1/TH2 balance of an immune response in favor of a TH2 response, by treatment of patient's cells in vivo or ex vivo. In the examples of the invention, a fusion protein comprising the extracellular domain of human Delta1 ligand fused to the Fc domain of human IgG4 was immobilized in microtiter plates via its Fc domain. CD4-pos. cell were cultured in the presence of the above fusion protein, stimulated with anti-CD28 antibody, and analyzed for cDNA expression by PCR. The CD4+ cells were restimulated in various ways and the cytokines IL-10 and interferon-γ were measured. Notch ligand signaling was also measured using a luciferase reporter construct in CHO cells cocultured with recombinant CHO cells expressing Delta1 ligand on the surface. Cytokine production was measured in stimulated mouse CD4+ cells under polarizing conditions. Transcription factor and cytokine expression by anti-CD3/28 activated mouse T cells activated under neutral, Th1, or Th2 culture conditions was measured with or without Delta1 protein.

L17 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2004:589350 Document No. 141:145678 Particle-bound modulators of the Notch signaling pathway for use in the treatment of disorders of the immune system. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; McKenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004060262 A2 20040722, 294 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB46 20040107. PRIORITY: GB 2003-234 20030107; GB 2003-1519 20030123; GB 2003-1510 20030123; GB 2003-1512 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1521 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1529 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-6621 20030322; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003.

AB Modulators of Notch signaling are immobilized on pharmaceutically acceptable carriers for therapeutic use in the treatment of immune disorders. Two derivs. of the Notch ligand Delta were prepared: a fusion protein with IgG4 and a cysteine-rich derivative These were immobilized on Dynabeads or polystyrene latex either by chemical crosslinking or by binding to an antibody to the IgG4 domain. The particle-bound ligands stimulated interleukin 10 secretion and inhibited interleukin 5 secretion in a mixed lymphocyte reaction using PBMCs from healthy donors.

L17 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2004:252539 Document No. 140:286167 Derivatives of Notch receptors ligand proteins for use as immunomodulators acting on T cells. Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara (Lorantis Limited, UK). PCT Int. Appl. WO 2004024764 A1 20040325, 145 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB3908 20030909. PRIORITY: GB 2002-20912 20020910; GB 2002-20913 20020910; WO 2002-GB5133 20021113; WO 2002-GB5137 20021113; GB 2003-234 20030107; WO 2003-GB1525 20030404; WO 2003-GB3285 20030801.

AB Derivs. of Notch receptors ligands, such as Delta-like 1, that include the DSL domain, 1-5 EGF repeat domains, and the N-terminal ligand domain fused to a second peptide are described for use in modifying an immune response. A series of derivs. of the Delta-like 1 Notch ligand containing 2-7 EGF repeats fused a human IgG Fc domain were constructed by standard methods. The shorter deletion derivs. were able to strongly induce a Notch signaling. Jagged-1 deletion derivs. antagonizing Notch signaling are also demonstrated.

L17 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
2004:162603 Document No. 140:210764 Modulation of immune function. Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert (Lorantis Limited, UK). PCT Int. Appl. WO 2004016279 A1 20040226, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB3556 20030813. PRIORITY: GB 2002-18879 20020814.
AB A method for modulating the immune system in a mammal is described comprising simultaneously, contemporaneously, sep. or sequentially administering: (i) an effective amount of a modulator of the Notch signaling pathway; and (ii) an effective amount of an interferon or a polynucleotide coding for an interferon.

L17 ANSWER 12 OF 20 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
2005:243154 The Genuine Article (R) Number: 855VO. The Notch ligand Delta modulates peripheral T-cell responses through two distinct pathways. Perry L C A (Reprint); Young L; Ballantyne S; Ward G A; Nye E; Watkins A; Rust A J; Lennard A C; Jennings L; Lioumi M; Tugal T; Dosanjh B; Sotheran E; Dillon J K; Ragno S; McKenzie G J; Champion B R. Lorantis Ltd, Cambridge, England. JOURNAL OF NEUROIMMUNOLOGY (SEP 2004) Vol. 154, No. 1-2, Sp. iss. SI, pp. 228-228. MA 755. ISSN: 0165-5728. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English.

L17 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
2005:242495 Document No. 142:428657 Notch signaling in the functional differentiation of peripheral CD4+ T-cells. McLaren, F. H.; Tan, K.; Champion, B.; Dallman, M.; Howie, S. E.; Lamb, J. R. (Immunobiology Group, MRC Centre for Inflammation Research, Respiratory Medicine Unit, Edinburgh University Medical School, Edinburgh, UK). Allergy Frontiers and Futures, Proceedings of the Symposium of the Collegium Internationale Allergologicum, 24th, Southampton, Bermuda, Nov. 1-7, 2002, Meeting Date 2002, 71-75. Editor(s): Bienenstock, John; Ring, Johannes; Togias, Alkis G. Hogrefe & Huber Publishers: Cambridge, Mass. ISBN: 0-88937-279-9 (English) 2004. CODEN: 69GPMM.
AB The Notch signaling pathway is a crucial regulator of cell fate decisions in many developmental systems, including T-cell development in the thymus. Recent evidence has established that components of the Notch pathway contribute to the regulation of peripheral immunity and T-cell function. To study the function of the Notch ligand Delta 1 in T-cells, the authors have generated transgenic mice with inducible expression targeted to T-cells. Transgenic mice were generated using the inducible Tet-On expression system, with expression of Delta 1 under the control of the human CD2 promoter. The cell-surface phenotype of peripheral CD4+ T-cells from transgenic mice was characterized by flow cytometry. In response to in vitro stimulation with anti-CD3/CD28 antibodies, the proliferative response of the transgenic T-cells was evaluated by measuring incorporation of tritiated thymidine, and cytokine profiles were determined by ELISA. The induction of the Delta 1 transgene in

CD4+ T-cells also resulted in enhanced levels of transcripts for Notch 4, Delta 3, Jagged 1, and Hes 1. Compared to controls, the cell surface phenotype of ex vivo transgenic peripheral CD4+ T-cells was unaltered, whereas following in vitro stimulation with anti-CD3/CD28, the expression of CD25 and CD69 was reduced. In addition to a decrease in IL-2 production, transgenic CD4+ T-cells produce higher levels of IL-10 after stimulation, compared to controls. The authors suggest that the Notch signaling pathway can contribute to functional differentiation of peripheral CD4+ T-cells and may be a potential therapeutic target for the treatment of allergic diseases.

L17 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:837139 Document No. 139:336935 Particle-bound Notch pathway-modifying immunomodulators for immunotherapy of cancer, allergy, infection, inflammation, and autoimmune disease and for modulator screening. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003087159 A2 20031023, 177 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB1525 20030404. PRIORITY: GB 2002-7930 20020405; GB 2002-7929 20020405; GB 2002-12282 20020528; GB 2002-12283 20020528; WO 2002-GB3397 20020725; WO 2002-GB3426 20020725; GB 2002-20913 20020910; GB 2002-20912 20020910; GB 2003-234 20030107.

AB A method is disclosed for therapeutic modulation of Notch signalling by administering modulators of the Notch signal transduction pathway bound to a pharmaceutically acceptable carrier. The modulators may be in mixts. of up to 100 different entities. The modulators may also be conjugated with one another, e.g. in fusion proteins. The construction of a CHO-derived cell line carrying a Notch pathway-dependent luciferase reporter gene to screen for Notch ligands is described.

L17 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:591212 Document No. 139:143996 Protein and cDNA sequences of human PDZ-RGS proteins and use in modulating Notch signalling pathway. Champion, Brian Robert; Falciani, Francesco; Hayward, Penelope Caroline; Maslen, Gareth Llewellyn (Lorantis Limited, UK). PCT Int. Appl. WO 2003062273 A2 20030731, 136 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB303 20030127. PRIORITY: GB 2002-1674 20020125.

AB The invention provides protein and cDNA sequences of human PDZ-RGS proteins. A method is described for modifying chemokine signalling by administering an effective amount of a modulator of the Notch signalling pathway. Human homologues of certain proteins, polypeptides and polynucleotides involved in Notch and/or chemokine signalling pathways are also described.

L17 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:396917 Document No. 138:396198 Fusion proteins comprising human Delta or Jagged proteins as inhibitors of the Notch signalling pathway and uses in cancer therapy. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew

Christopher; McKenzie, Grahame James; Ragno, Silvia; Tugal, Tamara; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003042246 A2 20030522, 217 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB5133 20021113. PRIORITY: GB 2001-27271 20011114; GB 2002-20913 20020910.

AB The present invention provides fusion proteins comprising human Delta protein or Jagged protein fused with IgG as inhibitors of the Notch signalling pathway and their therapeutic uses. Specifically, the invention provides (i) a protein or polypeptide which comprises a Notch ligand DSL domain and 0, 1 or 2 but no more than 2 Notch ligand EGF-like domains; (ii) a multimer of such a protein or polypeptide (wherein each monomer may be the same or different); or (iii) a polynucleotide coding for such a protein or polypeptide; for use in the treatment of cancer. The present invention seeks to provide further methods for treating cancer and, in particular, for promoting immune responses to cancer, in particular by modification of Notch-Notch ligand interaction.

L17 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:396736 Document No. 138:400396 Composition comprising inhibitors of Notch signaling pathway and pathogen antigen for vaccination against infection. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; McKenzie, Grahame James; Ragno, Silvia; Tugal, Tamara; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003041735 A2 20030522, 254 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB5137 20021113. PRIORITY: GB 2001-27267 20011114; WO 2002-GB3426 20020725; GB 2002-20849 20020907; GB 2002-20913 20020910; WO 2002-GB4390 20020927.

AB An inhibitor of the Notch signalling pathway is used in the manufacture of a medicament for use as an immunostimulant, for example as a vaccine adjuvant. The Notch ligand or receptor antagonists may comprise DSL domain of human Delta1, Delta3, or Delta4, extracellular domain of human Serrate or Jagged (Jagged 1 and 2), or EGF11 or EGF12 of human Notch1, Notch2, Notch3 or Notch4. These Notch inhibitors are capable of reducing the ability of Notch ligand to bind and/or activate Notch receptor on immune cells, and are capable of increasing activity of T cells, e.g. regulatory T cells, helper T cells, cytotoxic T lymphocytes, and effector T cells. The Notch signaling inhibitors are used in combination with antigen for vaccination against infection or chronic infection by pathogen such as bacteria, virus, fungus or parasite.

L17 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:282609 Document No. 138:302663 Immunomodulators modifying Notch signalling pathway for immunotherapy and modulator screening. Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Solari, Roberto Celeste Ercole (Lorantis Limited, UK). PCT Int. Appl. WO 2003029293 A2 20030410, 130 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB4390 20020927. PRIORITY: GB 2001-23379 20010928.

AB Use of a modulator of Notch IC protease activity in the manufacture of a medicament for use in immunotherapy and methods of detecting such a modulator. The Notch IC protease modulator includes agonist or antagonist of presenilin or presenilin-dependent γ-secretase. The Notch IC protease modulators are optionally in combination with Notch signalling pathway up-regulating agent (e.g. Notch ligands, Noggin, Chordin, follistatin, Xnr3, FGF and derivs.), or down-regulating agent (e.g. Toll-like receptor, cytokine, bone morphogenetic protein or BMP, BMP receptor, activin, or nucleic acid encoding them). The Notch signalling pathway modulators are useful for immunotherapy of allergy, inflammation, infection, autoimmune disease, graft rejection, cancer, and other T cell-mediated disease.

L17 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:118018 Document No. 138:168835 Targeting of an antigen presenting cell (APC) with a modulator of T cell signalling, such as a Notch ligand, coupled to the MHC class II-binding motif from a superantigen. Bodmer, Mark William; Champion, Brian Robert; McKenzie, Grahame James; Nye, Lucy Emma (Lorantis Limited, UK). PCT Int. Appl. WO 2003012111 A2 20030213, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3381 20020725. PRIORITY: GB 2001-18155 20010725.

AB The present invention relates to the concept of delivering a modulator of T cell signaling, such as a Notch ligand, to an antigen presenting cell (APC). The targeting approach disclosed uses, for example, the major histocompatibility complex (MHC) class II binding motif from a superantigen coupled to a modulator of the Notch signaling pathway. Superantigens bind both MHC class II mols. and subsets of T cell receptors and thus effectively cross-link APCs to T cells and activate cells polyclonally. The mol. regions of these mols. that impart T cell receptor (TCR) and MHC class II binding have been defined structurally and have been shown to be distinct regions of the mol. By using the MHC class II binding domain with a modulator of the Notch signaling pathway we can focus the activity of the Notch signaling pathway modulator to the APCs at the site of delivery. Further, the domain lacks toxin activity because it cannot find the T cell receptor to activate T cells. According to one aspect of the present invention there is provided a conjugate comprising a first and a second sequence wherein the first sequence comprises a polypeptide which is capable of binding to an APC, or a polynucleotide encoding therefor, and the second sequence comprises a polypeptide comprising a modulator of a signaling pathway in a T cell or a polynucleotide encoding therefor.

L17 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

2003:117645 Document No. 138:163535 Modulators of Notch signalling for use in immunotherapy. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003011317 A1 20030213, 182 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3426 20020725. PRIORITY: GB 2001-18153 20010725; GB 2002-7930 20020405; GB 2002-12282 20020528; GB 2002-12283 20020528.

AB The present invention provides new uses of modulators of Notch signaling in therapy and corresponding methods of treatment. The modulators of Notch signaling can be used to modulate immune cytokine expression in various cells for treatment of various diseases.

=> s l15 and conjugate
L18 17 L15 AND CONJUGATE

=> dup remove l18
PROCESSING COMPLETED FOR L18
L19 12 DUP REMOVE L18 (5 DUPLICATES REMOVED)

=> d l19 1-12 cbib abs

L19 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
2006:9689 Document No. 144:86546 Conjugates of Notch signaling modulators with supports for modulation of Notch signaling. Bodmer, Mark William; Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara; Ward, George Albert (UK). U.S. Pat. Appl. Publ. US 2006002924 A1 20060105, 129 pp., Cont.-in-part of Appl. No. PCT/GB03/03285. (English). CODEN: USXXCO. APPLICATION: US 2005-50346 20050203. PRIORITY: GB 2002-18068 20020803; GB 2002-20849 20020907; GB 2002-20912 20020910; GB 2002-20913 20020910; WO 2002-GB5137 20021113; WO 2002-GB5133 20021113; GB 2003-234 20030107; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801.

AB Conjugates comprising a plurality of modulators of the Notch signaling pathway chemical bound to a support structure are described. The conjugates are useful for modulation of the Notch signaling pathway. Thus, a human Delta 1 variant comprising amino acids 1-332 (the DSL domain and first 3 EGF repeats) and an addnl. cysteine at the C-terminus was prepared with recombinant mammalian cells. This protein was conjugated to sulfo-SMMC-activated amino dextran. Modulation of Notch signaling by this construct was demonstrated in cells and in mice.

L19 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
2004:802820 Document No. 141:312934 Vaccines comprising polynucleotide encoding Notch signalling modulator and antigen or antigenic determinant for medical treatment. Champion, Brian Robert; Ragno, Silvia (Lorantis Limited, UK). PCT Int. Appl. WO 2004083372 A2 20040930, 278 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB1229 20040322. PRIORITY: GB 2003-6583 20030321; GB 2003-6582 20030321; GB 2003-6621 20030322; GB 2003-6622 20030322; GB 2003-6626 20030322; GB 2003-6624 20030322; GB 2003-6640 20030322; GB 2003-6644 20030322; GB 2003-6650 20030322; GB 2003-6651 20030322; GB 2003-6654 20030322.

AB The invention provides a particle capable of being inserted into or taken up by a cell comprising (i) a polynucleotide coding for a modulator of Notch signalling; and (ii) a polynucleotide coding for an antigen or antigenic determinant thereof. The Notch signalling modulator is Delta or Serrate/Jagged protein, fragment, derivative, homolog, analog or allelic

variant. The antigen is an allergen, autoantigen, MHC antigen, or tumor antigen. The cell is immune cell, antigen-presenting cell, dendritic cell or Langerhans cell. Methods for using the particles are also described.

L19 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
2004:718374 Document No. 141:242022 Modulators of Notch signalling and of immune cell costimulatory activity for immunotherapy of inflammation, asthma, allergy, transplant rejection, graft versus host disease or autoimmune disease. Champion, Brian Robert; Lioumi, Maria; McKenzie, Grahame James (Lorantis Limited, UK). PCT Int. Appl. WO 2004073732 A1 20040902, 157 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB668 20040218. PRIORITY: GB 2003-3663 20030218.

AB A method is described for detecting, measuring or monitoring Notch signaling by determining the amount of an immune cell costimulatory protein, polypeptide or polynucleotide or determining the amount of a polynucleotide coding for such a protein or polypeptide. The Notch signaling modulators of the invention comprise Notch ligand DSL domain or intracellular domain. The immune cell costimulatory proteins are CD28, CD80, CD86, CTLA-4, ICOS, ICOS ligand, CD40, CD40L, PD-1, PD-L1, PD-L2, OX40 or OX40L. Methods of modulating the immune system are also described. The Notch signaling modulators and the immune cell costimulatory activity modulators are useful for increasing or reducing immune response against cancer or inflammation, allergy, asthma, graft vs. host disease, autoimmune disease and transplant rejection.

L19 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
2004:633546 Document No. 141:179617 Treatment of autoimmune diseases using an activator for the notch signaling pathway. Champion, Brian Robert; Ragno, Silvia; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004064863 A1 20040805, 244 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB263 20040123. PRIORITY: GB 2003-1519 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1512 20030123; GB 2003-1510 20030123; GB 2003-1521 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-1529 20030123; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003; WO 2004-GB46 20040107.

AB A product is disclosed comprising a modulator of the Notch signaling pathway; and an autoantigen or bystander antigen, or a polynucleotide coding for an autoantigen or bystander antigen; as a combined preparation for simultaneous, contemporaneous, sep. or sequential use for modulation of immune response. The invention relates to modulators of notch signalling pathway for T cell activation, and therapeutic use in immunosuppression. In the examples of the invention, a fusion protein comprising the extracellular domain of human Delta1 ligand fused to the Fc domain of human IgG4.

L19 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
2004:589350 Document No. 141:145678 Particle-bound modulators of the Notch

signaling pathway for use in the treatment of disorders of the immune system. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; McKenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2004060262 A2 20040722, 294 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ. (English). CODEN: PIXXD2. APPLICATION: WO 2004-GB46 20040107. PRIORITY: GB 2003-234 20030107; GB 2003-1519 20030123; GB 2003-1510 20030123; GB 2003-1512 20030123; GB 2003-1522 20030123; GB 2003-1524 20030123; GB 2003-1521 20030123; GB 2003-1518 20030123; GB 2003-1515 20030123; GB 2003-1513 20030123; GB 2003-1529 20030123; GB 2003-1526 20030123; GB 2003-1527 20030123; GB 2003-6621 20030322; WO 2003-GB1525 20030404; GB 2003-12062 20030524; WO 2003-GB3285 20030801; GB 2003-23130 20031003.

AB Modulators of Notch signaling are immobilized on pharmaceutically acceptable carriers for therapeutic use in the treatment of immune disorders. Two derivs. of the Notch ligand Delta were prepared: a fusion protein with IgG4 and a cysteine-rich derivative These were immobilized on Dynabeads or polystyrene latex either by chemical crosslinking or by binding to an antibody to the IgG4 domain. The particle-bound ligands stimulated interleukin 10 secretion and inhibited interleukin 5 secretion in a mixed lymphocyte reaction using PBMCs from healthy donors.

L19 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

2004:252539 Document No. 140:286167 Derivatives of Notch receptors ligand proteins for use as immunomodulators acting on T cells. Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara (Lorantis Limited, UK). PCT Int. Appl. WO 2004024764 A1 20040325, 145 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB3908 20030909. PRIORITY: GB 2002-20912 20020910; GB 2002-20913 20020910; WO 2002-GB5133 20021113; WO 2002-GB5137 20021113; GB 2003-234 20030107; WO 2003-GB1525 20030404; WO 2003-GB3285 20030801.

AB Derivs. of Notch receptors ligands, such as Delta-like 1, that include the DSL domain, 1-5 EGF repeat domains, and the N-terminal ligand domain fused to a second peptide are described for use in modifying an immune response. A series of derivs. of the Delta-like 1 Notch ligand containing 2-7 EGF repeats fused a human IgG Fc domain were constructed by standard methods. The shorter deletion derivs. were able to strongly induce a Notch signaling. Jagged-1 deletion derivs. antagonizing Notch signaling are also demonstrated.

L19 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

2003:837139 Document No. 139:336935 Particle-bound Notch pathway-modifying immunomodulators for immunotherapy of cancer, allergy, infection, inflammation, and autoimmune disease and for modulator screening. Bodmer, Mark William; Briend, Emmanuel Cyrille Pascal; Champion, Brian Robert; Lennard, Andrew Christopher; Mckenzie, Grahame James; Tugal, Tamara; Ward, George Albert; Young, Lesley Lynn (Lorantis Limited, UK). PCT Int. Appl. WO 2003087159 A2 20031023, 177 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB1525 20030404. PRIORITY: GB 2002-7930 20020405; GB 2002-7929 20020405; GB 2002-12282 20020528; GB 2002-12283 20020528; WO 2002-GB3397 20020725; WO 2002-GB3426 20020725; GB 2002-20913 20020910; GB 2002-20912 20020910; GB 2003-234 20030107.

AB A method is disclosed for therapeutic modulation of Notch signalling by administering modulators of the Notch signal transduction pathway bound to a pharmaceutically acceptable carrier. The modulators may be in mixts. of up to 100 different entities. The modulators may also be conjugated with one another, e.g. in fusion proteins. The construction of a CHO-derived cell line carrying a Notch pathway-dependent luciferase reporter gene to screen for Notch ligands is described.

L19 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

2003:118018 Document No. 138:168835 Targeting of an antigen presenting cell (APC) with a modulator of T cell signalling, such as a Notch ligand, coupled to the MHC class II-binding motif from a superantigen. Bodmer, Mark William; Champion, Brian Robert; McKenzie, Grahame James; Nye, Lucy Emma (Lorantis Limited, UK). PCT Int. Appl. WO 2003012111 A2 20030213, 93 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3381 20020725. PRIORITY: GB 2001-18155 20010725.

AB The present invention relates to the concept of delivering a modulator of T cell signaling, such as a Notch ligand, to an antigen presenting cell (APC). The targeting approach disclosed uses, for example, the major histocompatibility complex (MHC) class II binding motif from a superantigen coupled to a modulator of the Notch signaling pathway. Superantigens bind both MHC class II mols. and subsets of T cell receptors and thus effectively cross-link APCs to T cells and activate cells polyclonally. The mol. regions of these mols. that impart T cell receptor (TCR) and MHC class II binding have been defined structurally and have been shown to be distinct regions of the mol. By using the MHC class II binding domain with a modulator of the Notch signaling pathway we can focus the activity of the Notch signaling pathway modulator to the APCs at the site of delivery. Further, the domain lacks toxin activity because it cannot find the T cell receptor to activate T cells. According to one aspect of the present invention there is provided a conjugate comprising a first and a second sequence wherein the first sequence comprises a polypeptide which is capable of binding to an APC, or a polynucleotide encoding therefor, and the second sequence comprises a polypeptide comprising a modulator of a signaling pathway in a T cell or a polynucleotide encoding therefor.

L19 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

2002:927470 Document No. 138:23680 Modulation of immune responses by modulation of the Notch signaling pathway and use of transport proteins to transport modulators into cells. Solari, Roberto Celeste Ercole; Champion, Brian Robert; Ward, George Albert (Lorantis Limited, UK). PCT Int. Appl. WO 2002096952 A2 20021205, 80 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW;

RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB2438 20020524. PRIORITY: GB 2001-12818 20010525.

AB A method of modulating the immune response by activating or inhibiting the Notch signal transduction pathway is described. The method uses a conjugate of a transport protein and a Notch pathway-regulating moiety, such as a protein or an oligonucleotide that either up-regulates or down-regulates the pathway. The effector protein may be derived from a natural regulator of the pathway, such as a domain of the Notch receptor, or it may be a ligand such as an antibody.

L19 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 1

92143791. PubMed ID: 1736881. Expression, purification and characterization of a mouse-human chimeric antibody and chimeric Fab' fragment. King D J; Adair J R; Angal S; Low D C; Proudfoot K A; Lloyd J C; Bodmer M W; Yarranton G T. (Celltech Ltd., Berks, U.K.) The Biochemical journal, (1992 Jan 15) Vol. 281 (Pt 2), pp. 317-23. Journal code: 2984726R. ISSN: 0264-6021. Pub. country: ENGLAND: United Kingdom. Language: English.

AB B72.3 is a mouse monoclonal antibody against a tumour-associated antigen, TAG72, which recognizes breast, ovarian and colorectal tumour tissue. A mouse-human chimeric version of B72.3 has been expressed in Chinese-hamster ovary cells. This molecule has the binding specificity of B72.3 and constant regions from human IgG4. The chimeric B72.3 assembles to intact IgG and recognizes TAG72 as well as B72.3 in competitive binding assays. A proportion of the chimeric B72.3 (approx. 10%) does not form inter-heavy-chain disulphide bonds but still assembles into the IgG tetramer. This appears to be a general property of human IgG4 molecules. Co-expression of the chimeric light chain with a chimeric Fd' gene resulted in the expression of functional Fab'. Very little F(ab')2 is produced, although the Fab' can be oxidized to the dimeric F(ab')2 in vitro. The production of Fab' and F(ab')2 by this method is an attractive alternative to proteolytic digestion of IgG. The ability to produce these molecules in large quantities will allow the production and testing of a range of anti-tumour antibody and antibody fragment conjugates.

L19 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 2

89094680. PubMed ID: 3210137. Rapid and simple synthesis for the sulphate esters of 6-hydroxy-melatonin and N-acetyl-serotonin. Leone A M; Francis P L; McKenzie-Gray B. (Department of Reproductive Physiology, St. Bartholomew's Hospital, Medical College, London.) Journal of pineal research, (1988) Vol. 5, No. 4, pp. 367-71. Journal code: 8504412. ISSN: 0742-3098. Pub. country: United States. Language: English.

AB Melatonin is metabolised by hydroxylation at the 6 position and to a variable extent by demethylation. Both metabolites so formed are excreted as sulphate and, to a lesser extent, glucuronide conjugates. To authenticate these metabolites which we had earlier isolated from urine, we wished to have synthetic samples. Since we also required them as standards we needed them as powders. A review of the literature showed that there were only two published methods, of which only one gave rise to 6-sulphatoxy-melatonin (SaMT) as a solid. The other metabolite, N-acetyl-serotonin-sulphate (SNAS), has not been previously made, and we here describe some of its chemical properties. Our method modifies a published method taking into account the results given in a recent paper describing the sulphation of the thyroid hormones, T3 and T4. Hydroxy-melatonin is thus reacted with a complex formed from dimethylformamide and chlorosulphonic acid. The reaction is of interest since it is rapid, easy, and produces pure powdered material in excellent yield.

L19 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

1976:474500 Document No. 85:74500 Solid-phase, magnetic particle radioimmunoassay. Nye, Lynn; Forrest, G. C.; Greenwood, Helena; Gardner, Jaqueline S.; Jay, R.; Roberts, J. R.; Landon, J. (Dep. Chem.

Pathol., St. Bartholomew's Hosp., London, UK). Clinica Chimica Acta, 69(3), 387-96 (English) 1976. CODEN: CCATAR. ISSN: 0009-8981.

AB A solid-phase radioimmunoassay system was developed that is based on the use of antibodies covalently linked to polymer-coated iron oxide (Enzacryl). An electromagnet is used both to mix the particles during incubation and to sep. the antibody-bound and free fractions. This obviates the need for vertical rotation and for the time-consuming, multiple centrifugations required with conventional solid-phase procedures. The system is applicable universally, and methods were established for the assay of thyroxine, human placental lactogen, and digoxin. The thyroxine assay was used as a model, and it was shown that the results obtained for serum samples correlated closely with those by using a routine liquid-phase radioimmunoassay. The applicability of employing a 2nd antibody linked to the iron oxide particles also was studied.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	212.45	212.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-36.75	-36.75

STN INTERNATIONAL LOGOFF AT 18:38:34 ON 12 JUL 2006